

**REMARKS**

Claims 17-21 are currently pending. By the present communication, no claims have been added or canceled, and claim 18 has been amended to define Applicants' invention with greater particularity. Support for the amendments can be found throughout the application as filed. Accordingly, the amendments do not raise any issue of new matter.

**Rejection under 35 U.S.C. §112, First Paragraph**

Applicants respectfully traverse the rejection of claims 17- 21 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Office indicates that

Nowhere in the application as filed, does applicant literally recite detecting the presence of the foreign gene transferred to the second cell as a result of contact infiltration from the first cell. Additionally, nowhere in the instant application does applicant provide the protocols necessary for the skilled artisan to differentiate the second cell from the first and specifically detect the presence of the foreign gene in the second cell. (Office Action, page 3, lines 5-10).

Applicants respectfully submit that M.P.E.P. §2163 provides that, “[w]hile there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure.” Accordingly, “literal” support is not necessary for fulfilling the written description requirement.

As recited in the preamble of claim 17, the method of the present invention relates to the transfer of a foreign gene from a first cell to a second cell through contact infiltration. Needless to say, this invention is based on the findings of this transfer. In other words, this invention could not have been made without detecting the transfer. Applicants respectfully direct the Examiner's attention to Example 6 of the specification as filed, which demonstrates that the inventors detected the transfer. As such, the amended claim is supported by the specification, at least expressly, implicitly, or inherently.

The Office further states that, “nowhere in the instant application does applicant provide the protocols necessary for the skilled artisan to differentiate the second cell from the first and

specifically detect the presence of the foreign gene in the second cell.” Applicants respectfully submit that the presence of the foreign gene can be detected by conventional techniques, for example, by detecting the expansion of the virus vector as described in the specification (see, e.g., Example 6). Moreover, M.P.E.P. §2163 states that, “[w]hat is conventional or well known to one of ordinary skill in the art need not be disclosed in detail.” The Examiner himself states that, “[o]nce the ordinary skilled artisan sought to detect the presence of the foreign gene in the second cell, he/she would have been able to select from numerous procedures for detecting gene transfer” (Office Action, paragraph bridging pages 5-6). The Examiner further states that, “[t]he ordinary skilled artisan could use any of numerous gene transfer detection systems” (page 6, lines 5-6). As such, Applicants submit that one of ordinary skill in the art would have been able to select from a plethora of conventional techniques for differentiating the second cell from the first, and more specifically detecting the presence of the foreign gene in the second cell. Accordingly, Applicants assert that detailed protocols do not need to be provided in the specification, and request withdrawal of the rejection.

### **Rejection under 35 U.S.C. §103**

Applicants respectfully traverse the rejection of claims 17-21 under 35 U.S.C. §103(a) as allegedly being unpatentable over Nagai et al. (hereinafter, “Nagai”) in view of Zhang et al. (hereinafter, “Zhang”) or Nable et al. (hereinafter, “Nable”). Specifically, the Office indicates that,

Nagai et al. teaches the essential features of the claimed invention with the exception of detecting the gene(s) transferred to the second cell by the inoculated first cell. The question therefore is whether it would have been obvious for the ordinary skilled artisan to monitor transfer of the gene(s) of interest to the second cell. The answer must be yes because the purpose of the protocols disclosed by Nagai et al. is the transfer genes to target cells and said skilled artisan would of course seek to determine whether the transfer had been successful. (Office Action, page 5, lines 5-11).

The Examiner further states that,

The ordinary skilled artisan...would have been motivated to detect the presence of the foreign gene in the second cell *to determine whether the transfer had been successful* as

one could not automatically assume that successful transfer had occurred. Once the ordinary skilled artisan sought to detect the presence of the foreign gene in the second cell, he/she would have been able to select from numerous procedures for detecting gene transfer, for example the use of GFP (as a gene transfer marker) as recited by Zhang et al. or use of Southern blotting to detect the presence of the transferred DNA (as recited by Nabel et al.). It would have been obvious for the ordinary skilled artisan to detect the presence of the foreign gene in the second cell because this would confirm that the foreign gene *was transferred successfully*. . . . Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be considered that said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention. (Office Action, paragraph bridging pages 5 and 6, emphasis added).

Applicants submit that the Examiner's arguments rely on the assumption that the skilled artisan would have recognized that the gene transfer from the first cell to the second cell is merely a "success" of the use of the conventional viral vector, and he/she would have "expected" this transfer. However, none of Nagai, Zhang, or Nabel supports this assumption. It is true that Nagai et al. describe "a complex..., having the cell infectivity and capable of autonomously replicating RNA, but deficient in the disseminative capability" (Claim 1 of Nagai). Such a complex may comprise an RNA molecule defective in one or more of M, F, and HN genes (Claim 5 of Nagai). However, Nagai is absolutely silent with regard to the ability of a specific species of virus to expand the transgene from the infected cell to the neighboring cell through cell-to-cell contact (*i.e.*, contact infiltration). Rather, Nagai expressly describes that, "[s]ince said complexes can replicate *only within infected cells* but not spread *from cell to cell*, these techniques are especially useful in the fields of gene therapy, etc. wherein therapeutical safety is highly appreciated." (Nagai, page 15, lines 3-4, emphasis added). Accordingly, Nagai teaches away from the present invention.

Applicants respectfully submit that the transfer of a gene from the first cell to the second cell is not a "success" of the use of a conventional vector. Therefore, a skilled artisan would not have been motivated to detect the presence of the foreign gene in the second cell to determine whether the transfer had been successful. More importantly, a skilled artisan would NOT have had a reasonable expectation of successfully detecting the presence of the foreign gene in the second cell.

Applicants respectfully submit that M.P.E.P. §2141.02 provides that, “[i]n determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious.” Further, M.P.E.P. §2143.03 provides that, “[a]ll words in a claim must be considered in judging the patentability of that claim against the prior art.” The Court in *In re Marshall* held that a compound’s known disadvantages, which would naturally discourage search for new uses of that compound, may be taken into account in determining obviousness (*In re Marshall*, 578 F.2d 301, 198 USPQ 344 (CCPA 1978)). In *Marshall* an Examiner cited the PHYSICIAN’S DESK REFERENCE (PDR), which listed multiple indications and dosages for a particular compound, against a use of the compound to control weight by turning off the production and release of pancreatic enzymes. The Court overturned the Examiner’s rejection, saying “nowhere in any reference is there any suggestion to control weight by turning off the production and release of pancreatic enzymes.... To say this would have been obvious is to resort to impermissible hindsight.” (*In re Marshall*, 578 F.2d at 347). As in *Marshall*, the references cited against the present invention are absolutely silent with regard to the ability of a specific species of virus to expand the transgene from the infected cell to the neighboring cell through cell-to-cell contact (*i.e.*, contact infiltration). In fact, Nagai expressly teaches away from the claimed invention by indicating that the complexes can “...replicate *only within infected cells* but not spread *from cell to cell*....” (Nagai, page 15, lines 3-4, emphasis added). Accordingly, the Office has not established a *prima facie* case against the claimed invention. Accordingly, withdrawal of the rejection is respectfully requested.

In re Application of:  
• Asakawa and Hasegawa  
Application No.: 09/762,641  
Filed: April 1, 2005  
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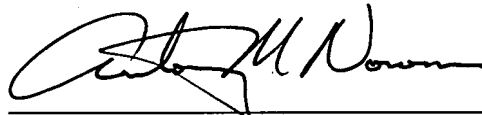
PATENT  
Attorney Docket No.: SHIM1100

### CONCLUSION

In summary, for the reasons set forth herein, Applicants respectfully submit that the claims clearly and patentably define the invention, and allowance of the claims is respectfully requested. If the Examiner would like to discuss any issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Check number 586107 in the amount of \$225.00 is enclosed as payment for the Petition for Two-Month Extension of Time fee. No other fee is believed to be due in connection with the filing of this paper. However, the Commissioner is hereby authorized to charge any fees that may be required by this paper, or credit any overpayment to Deposit Account 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal sheet is enclosed.

Respectfully submitted,



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